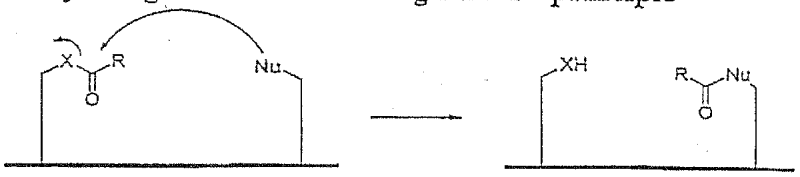
Fig. 6. Reaction types allowing simultaneous reaction and linker cleavage.

Nucleophilic substitution using activation of electrophiles

FIG. 6A. Acylating monomer building blocks - principle



X = O, S Nu = Oxygen-, Nitrogen-, Sulfur- and Carbon Nucleophiles

FIG. 6B. Acylation

Amide formation by reaction of amines with activated esters

FIG. 6C. Acylation

Pyrazolone formation by reaction of hydrazines with β–Ketoesters

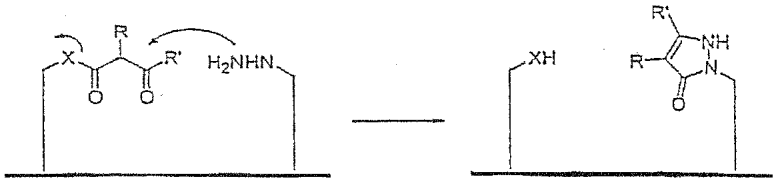


FIG. 6D. Acylation

Isoxazolone formation by reaction of hydroxylamines with β–Ketoesters

FIG. 6E. Acylation

Pyrimidine formation by reaction of thioureas with β–Ketoesters

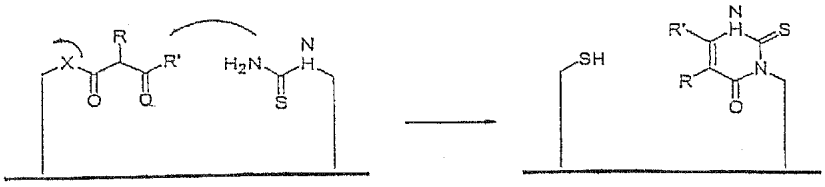


FIG. 6F. Acylation

Pyrimidine formation by reaction of ureas with Malonates

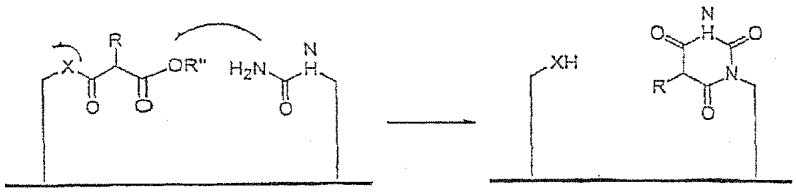


FIG. 6G. Acylation

Coumarine or quinolinon formation by a Heck reaction followed by a nucleophilic substitution

X = O,S X' = Halogen, OTf, OMs Z = O, NH

FIG. 6H. Acylation

Phthalhydrazide formation by reaction of Hydrazines and Phthalimides

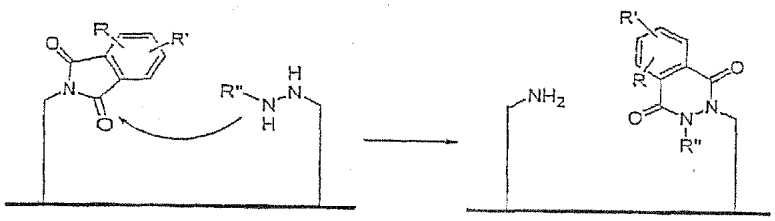
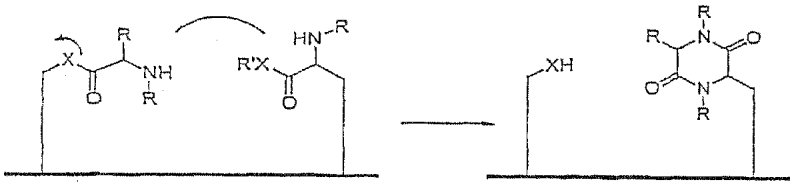


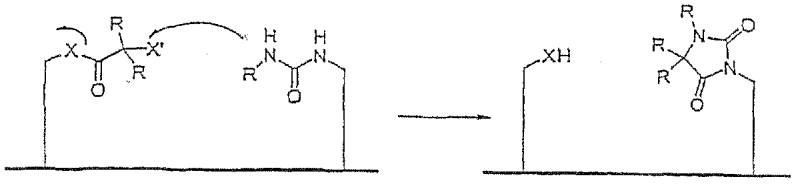
FIG. 6I. Acylation

Diketopiperazine formation by reaction of Amino Acid Esters



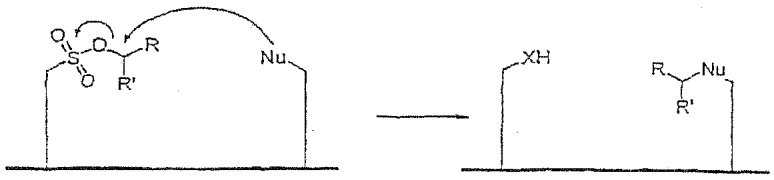
X = O, S R' = H, R

FIG. 6J. Acylation
Hydantoin formation by reaction of Urea and α-substituted Esters



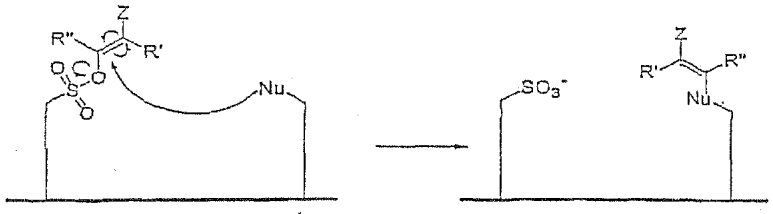
X = O, S X' = Hal, OTos, OMs, etc.

FIG. 6K. Alkylating monomer building blocks - principle
Alkylated compounds by reaction of Sulfonates with Nucleofiles



Nu = Oxygen- , Nitrogen- , Sulfur- and Carbon Nucleophiles

FIG. 6L. Vinylating monomer building blocks - principle



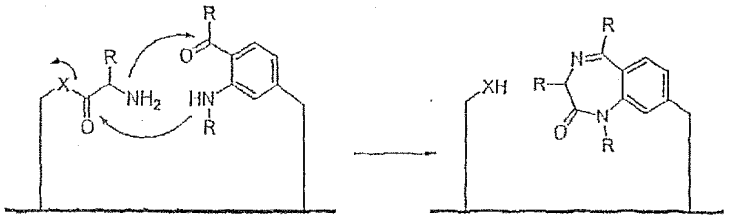
Z = CN, COOR, COR, NO_2, SO_2R, S(=O)R, SO_2NR_2, F
Nu = Oxygen- , Nitrogen- , Sulfur- and Carbon Nucleophiles

FIG. 6M. Heteroatom electrophiles

Disulfide formation by reaction of Pyridyl disulfide with mercaptanes

FIG. 6N. Acylation

Benzodiazepinone formation by reaction of Amino Acid Esters and Amino Ketones

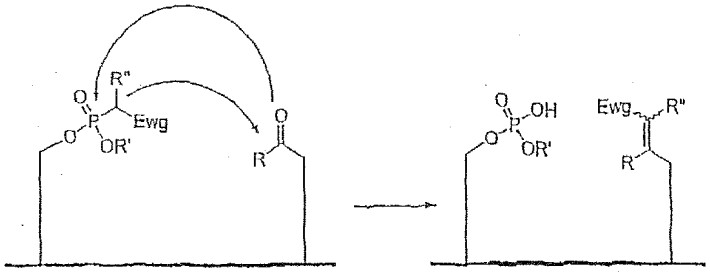


X = O, S

Addition to carbon-hetero multiple bonds

FIG. 6O. Wittig/Horner-Wittig-Emmons reagents

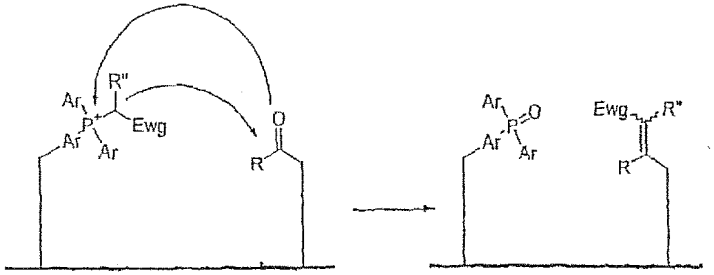
Substituted alkene formation by reaction of Phosphonates with Aldehydes or Ketones



Ewg = CN, COOR, COR, NO_2, SO_2R, S(=O)R, SO_2NR_2, F etc.

FIG. 6P. Wittig/Horner-Wittig-Emmons reagents

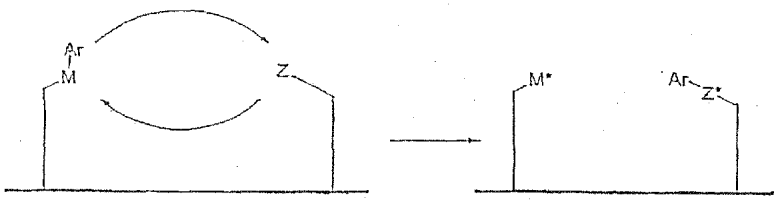
Substituted alkene formation by reaction of Phosphonates with Aldehydes or Ketones



Ewg = CN, COOR, COR, NO_2, SO_2R, S(=O)R, SO_2NR_2, F etc.
Ar = aryl, hetaryl

Transition metal catalysed reactions

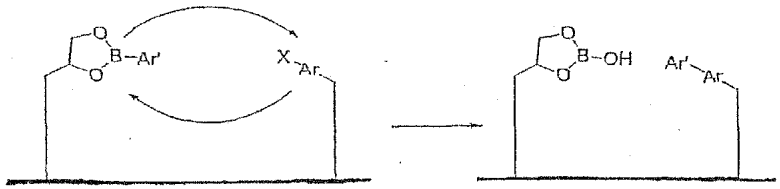
FIG. 6Q. Transition metal cat. Arylations



Z = haloaryl, halohetaryl, ArOMs, ArOTf, ArOTos or NHR or OH or SH etc.
Z* = Aryl, hetaryl, NR or O or S etc
M = e.g. BR, BR_2^-, SnR_2 etc.
R = H, alkyl, aryl, hetaryl, OR, NR_2
M* = e.g. B(OH)R, $B(OH)R_2^-$, $Sn(OH)R_2$ etc.

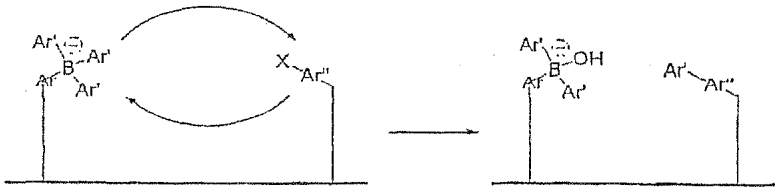
FIG. 6R. Arylation

Biaryl formation by the reaction of Borates with Aryls or Heteroaryls



X = Halogen, OMs, OTf, OTos, etc

FIG. 6S. Arylation
Biaryl formation by the reaction of Boronates with Aryls or Heteroaryls



X = Halogen, OMs, OTf, OTos, etc
Ar = aryl, hetaryl

FIG. 6T. Arylation
Biaryl formation by the reaction of Boronates with Aryls or Heteroaryls

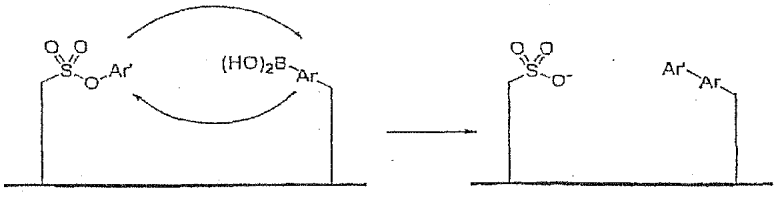


FIG. 6U. Arylation

Arylamine formation by the reaction of amines with activated Aryls or Heteroaryls

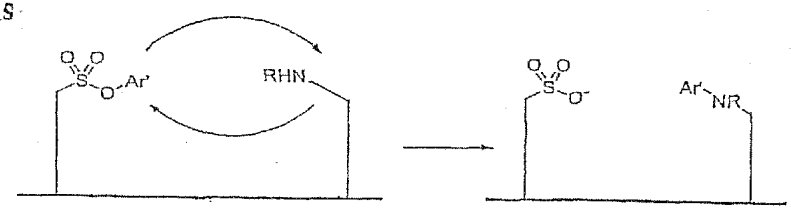


FIG. 6V. Arylation

Arylamine formation by the reaction of amines with hypervalent iodonium salts

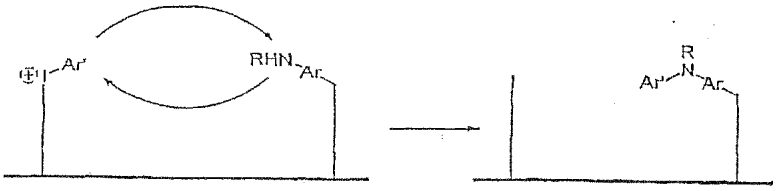
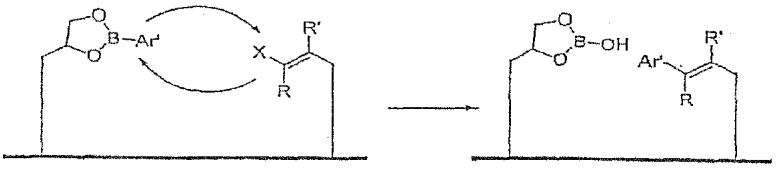


FIG. 6X. Arylation

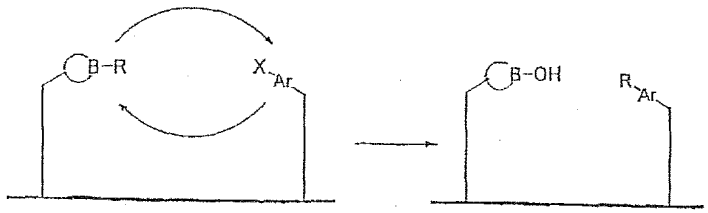
Vinylarene formation by the reaction of alkenes with Aryls or Heteroaryls



X = Halogen, OMs, OTf, OTos, etc

FIG. 6Y. Alkylation

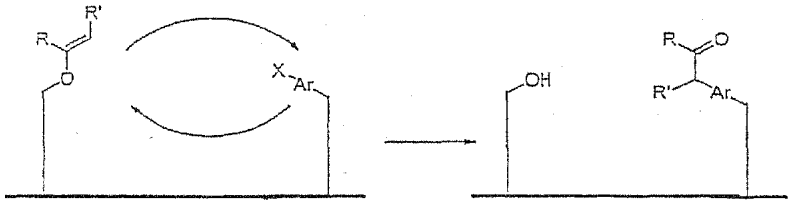
Alkylation of arenes/hetarens by the reaction with Alkyl boronates



X = Halogen, OMs, OTf, OTos, etc

FIG. 6Z. Alkylation

Alkylation of arenes/hetarenes by reaction with enolethers

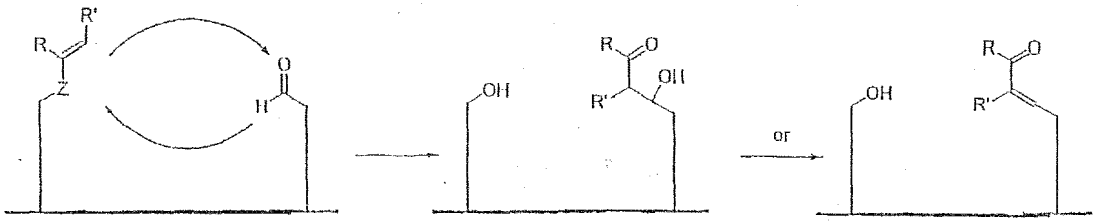


X = Halogen, OMs, OTf, OTos, etc

Nucleophilic substitution using activation of nucleophiles

FIG. 6AA. Condensations

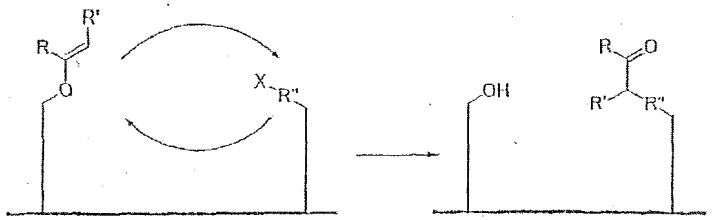
Alkylation of aldehydes with enolethers or enamines



Z = NR, O; X = Halogen, OMs, OTf, OTos, etc

FIG. 6AB. Alkylation

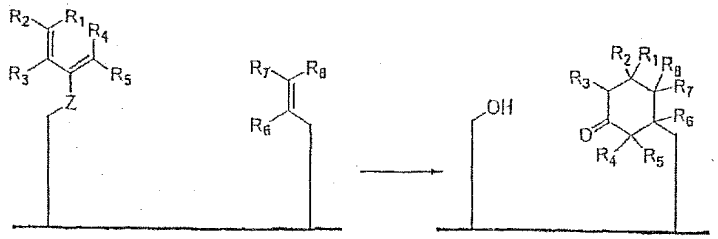
Alkylation of aliphatic halides or tosylates with enolethers or enamines



X = Halogen, OMs, OTf, OTos, etc

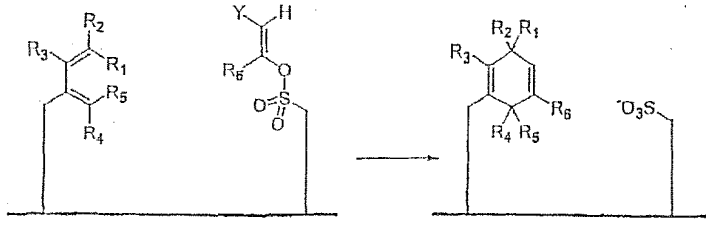
Cycloadditions

FIG. 6AC. [2+4] Cycloadditions



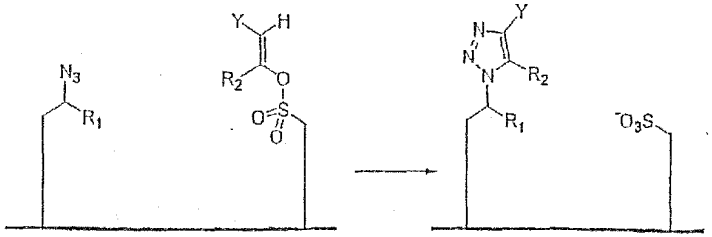
Z = O, NR

FIG. 6AD. [2+4] Cycloadditions



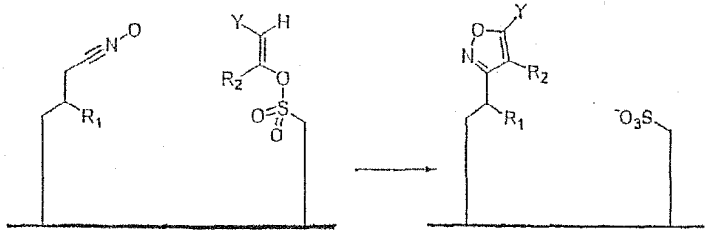
Y = CN, COOR, COR, NO_2, SO_2R, S(=O)R, SO_2NR_2, F

FIG. 6AE. [3+2] Cycloadditions



Y = CN, COOR, COR, NO_2, SO_2R, S(=O)R, SO_2NR_2, F

FIG. 6AF. [3+2] Cycloadditions



Y = CN, COOR, COR, NO_2, SO_2R, S(=O)R, SO_2NR_2, F

FIG. 7A . Pairs of reactive groups X,Y and the resulting bond XY.

Nucleophilic substitution reactions

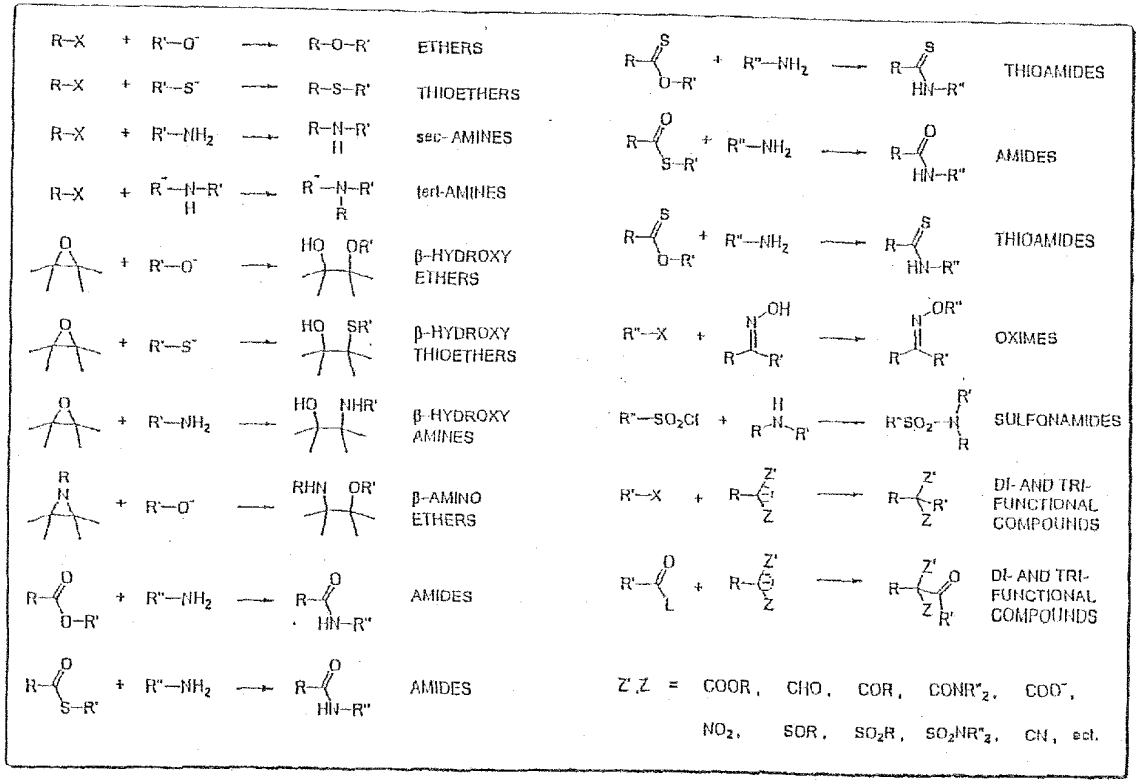


FIG. 7B

Aromatic nucleophilic substitution

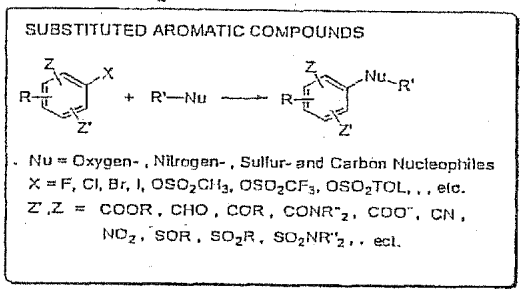


FIG. 7C

Transition metal catalysed reactions

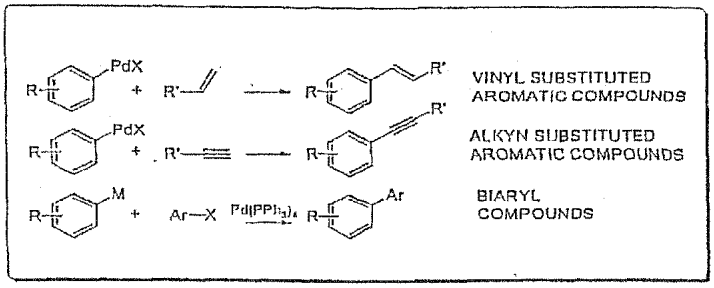


FIG. 7D Addition to carbon-carbon multiple bonds

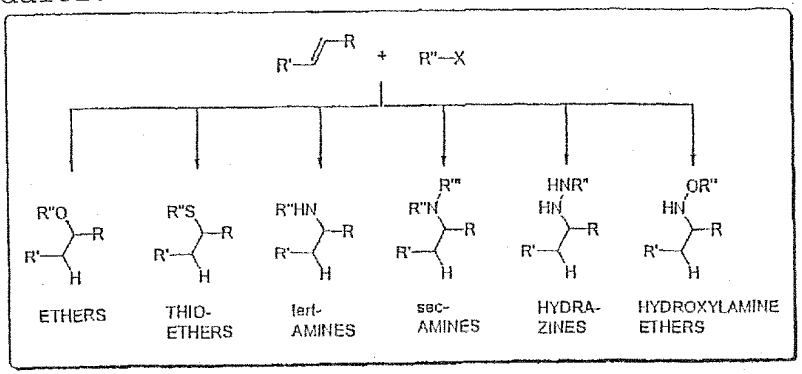


FIG. 7E

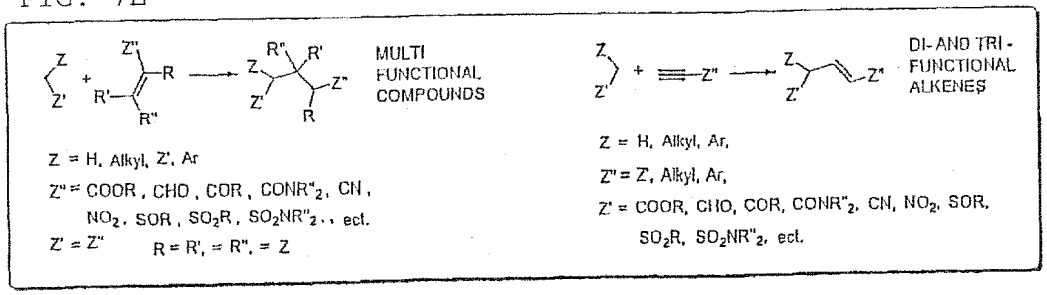


FIG. 7F Cycloaddition to multiple bonds

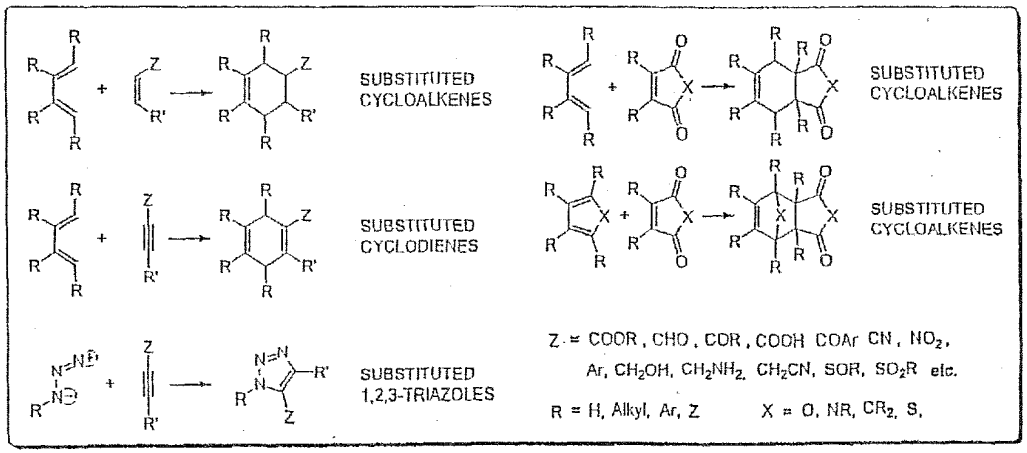


FIG. 7G Addition to carbon-hetero multiple bonds

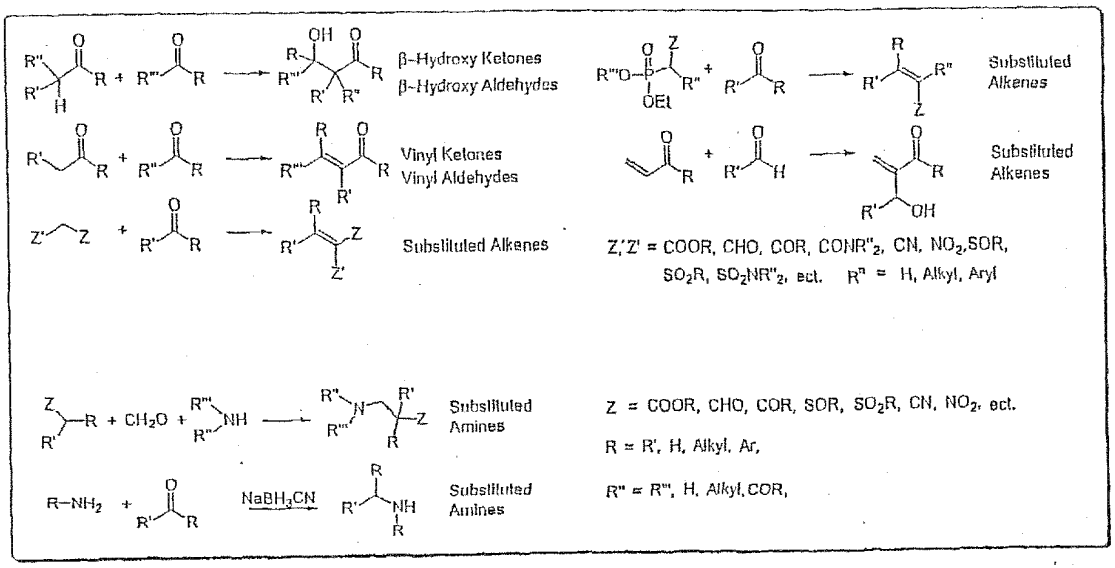


Figure 8. Cleavable Linkers

FIG. 8A. Linker for the formation of Ketones, Aldehydes, Amides and Acids

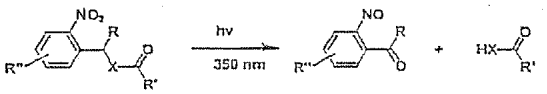


FIG. 8B. Linker for the formation of Ketones, Amides and Acids

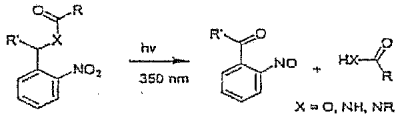


FIG. 8C. Linker for the formation of Aldehydes and Ketones

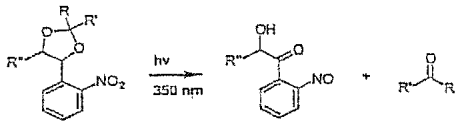


FIG. 8D. Linker for the formation of Alcohols and Acids

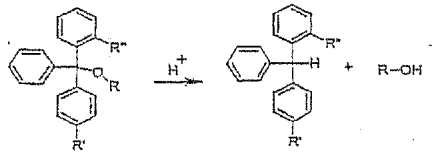


FIG. 8E. Linker for the formation of Amines and Alcohols

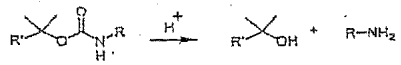


FIG. 8F. Linker for the formation of Esters, Thioesters, Amides and Alcohols

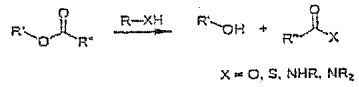


FIG. 8G. Linker for the formation of Sulfonamides and Alcohols

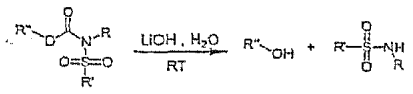


FIG. 8H. Linker for the formation of Ketones, Amines and Alcohols

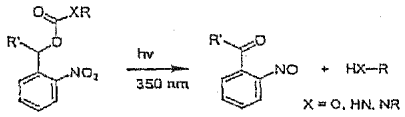


FIG. 8I. Linker for the formation of Ketones, Amines, Alcohols and Mercaptanes

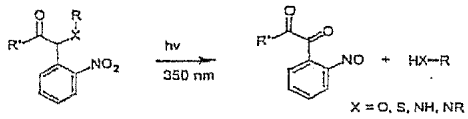


FIG. 8J. Linker for the formation of Biaryl and Bihetaryl

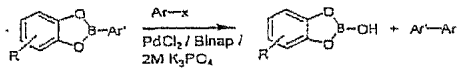


FIG. 8K. Linker for the formation of Benzyles, Amines, Anilins Alcohols and Phenoles

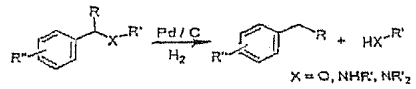
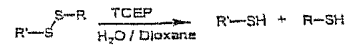


FIG. 8L. Linker for the formation of Mercaptanes



TCEP = tris(2-carboxyethyl)phosphine

FIG. 8M. Linker for the formation of Glycosides

FIG. 8N. Linker for the formation of Aldehydes and Glyoxylamides

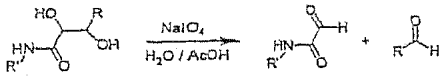


FIG. 8O. Linker for the formation of Aldehydes, Ketones and Aminoalcohols

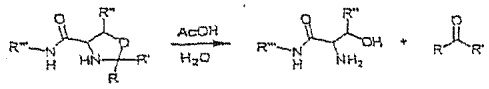


Figure 9

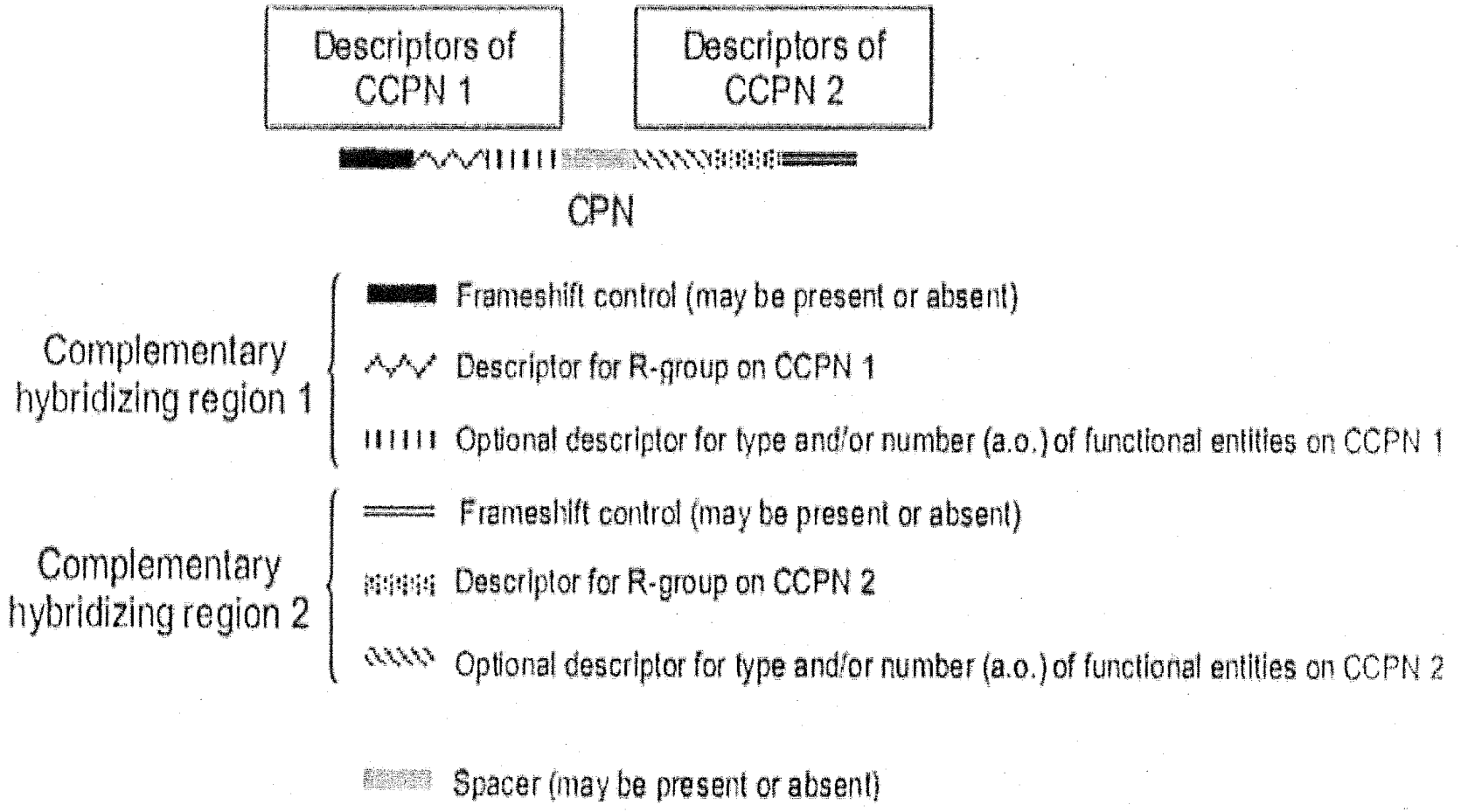
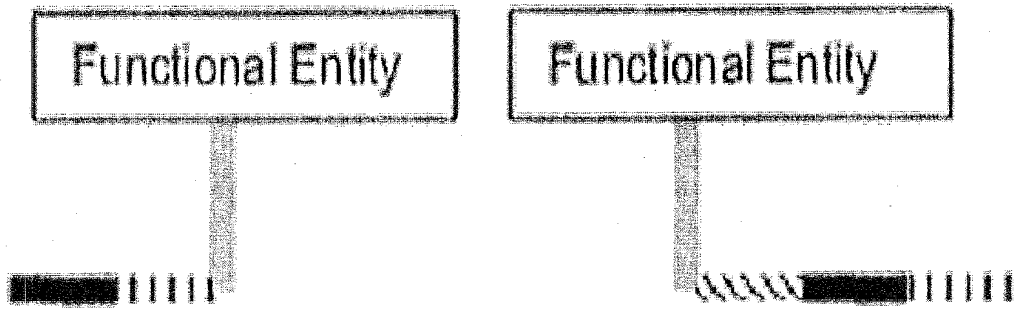

Descriptors of CCPN 1
Descriptors of CCPN 2
CPN
Complementary hybridizing region 1
Frameshift control (may be present or absent)
Descriptor for R-group on CCPN 1
Optional descriptor for type and/or number (a.o.) of functional entities on CCPN 1
Complementary hybridizing region 2
Frameshift control (may be present or absent)
Descriptor for R-group on CCPN 2
Optional descriptor for type and/or number (a.o.) of functional entities on CCPN 2
Spacer (may be present or absent)

Figure 10



CCPN containing one hybridizing region

CCPN containing two hybridizing regions

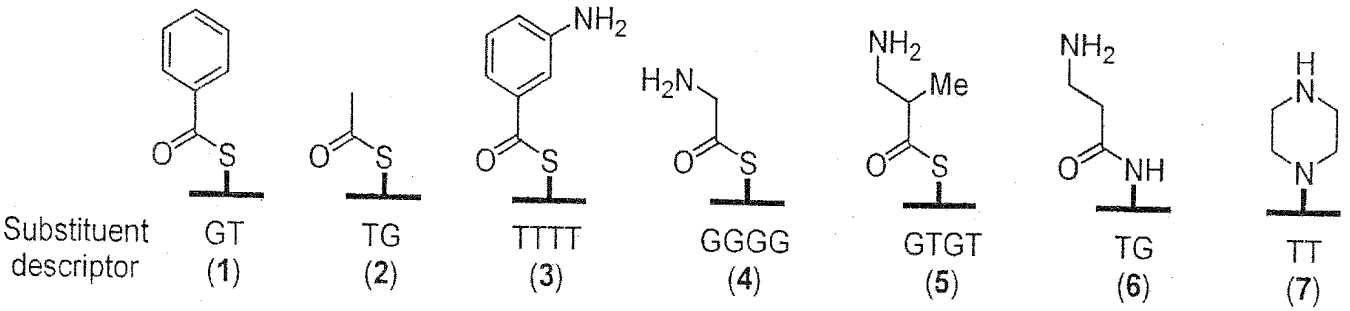
Descriptor for substituent or scaffold type (a.o.) -CCPN compo-

Optional call or answer region – signalering in which context this CCPN is allowed

Optional call or answer region – signalering in which context this CCPN is allowed

Linker

FIG. 11


Substituent descriptor
GT (1)
TG (2)
TTTT (3)
GGGG (4)
GTGT (5)
TG (6)
TT (7)
BB1
BB2
3'-answer
call-5'
3'-answer
call-5'
5'-call*
answer*-3'
CPN